WEST

Generate Collection Print

L9: Entry 6 of 14 File: USPT Jun 17, 1997

DOCUMENT-IDENTIFIER: US 5639608 A
TITLE: Method for sequencing DNA using a T7-type DNA polymerase and short oligonucleotide primers

Brief Summary Text (8):
In preferred embodiments the polymerase remains bound to the DNA molecule for at least 1000 bases before dissociating; the polymerase is substantially the same as one in cells infected with a T7-type phase (i.e., phage in which the DNA polymerase requires host thioredoxin as a subunit; for example, the T7-type phage is T7, T3, .phi.I, .phi.II, H, W31, gh-1, Y, All22, or SP6, Studier, 95 Virology 70, 1979); the polymerase is non-discriminating for dideoxy nugleotide analogs; the polymerase is modified to have less than 50 units of exonuclease activity per mg of polymerase, more preferably less than 1 unit, even more preferably less than 0.1 unit, and most preferably has no detectable exonuclease activity; the polymerase is able to utilize primers of as short as 10 bases or preferably as short as 4 bases; the primer comprises four to forty nucleotide bases, and is single stranded DNA or RNA; the annealing step comprises heating the DNA molecule and the primer to above 65.degree. C., preferably from 65.degree. C. to 100.degree. C., and allowing the heated mixture to cool to below 65.degree. C, preferably to 0.degree. C. to 30.degree. C.; the incubating step comprises a pulse and a chase step, wherein the pulse step comprises mixing the annealed mixture with all four different deoxynucleoside triphosphates and a processive DNA polymerase wherein at least one of the deoxynucleoside triphosphates is labelled; most preferably the pulse step performed under conditions in which the polymerase does not exhibit its processivity and is for 30 seconds to 20 minutes at 0.degree. C. to 20.degree. C. or where at least one of the nucleotide triphosphates is limiting; and the chase step comprises adding one of the chain terminating agents to four separate aliquots of the mixture after the pulse step; preferably the chase step is for 1 to 60 minutes at 30.degree. C. to 50.degree. C.; the terminating agent is a dideoxynucleotide, or a limiting level of one deoxynucleoside triphosphate; one of the four deoxynucleotides is dITP or deazaquanosine; labelled primers are used so that no pulse step is required, preferably the label is radioactive or fluorescent; and the polymerase is unable to exhibit its processivity in a second environmental condition normally used in the pulse reaction of a DNA sequencing reaction.

Detailed Description Text (16):
DNA polymerases of this invention, (i.e., having the above properties) include modified T7-type polymerases. That is the DNA polymerase requires host thioredoxin as a sub-unit, and they are substantially identical to a modified T7 DNA polymerase or to equivalent enzymes isolated from related phage, such as T3, .phi.I, .phi.II, H, W31, gh-1, Y, All22 and SP6. Each of these enzymes can be modified to have properties similar to those of the modified T7 enzyme. It is possible to isolate the enzyme from phage infected cells directly, but preferably the enzyme is isolated from cells which overproduce it. By substantially identical is meant that the enzyme may have amino acid substitutions which do not affect the overall properties of the enzyme. One example of a particularly desirable amino acid substitution is one in which the natural enzyme is modified to remove any exonuclease activity. This modification may be performed at the genetic or chemical level (see below).

Detailed Description Text (109):
In order to sequence through regions of compression in DNA, i.e., regions having compact secondary structure, it is common to use dITP (Mills et al., 76 Proc. Natl.

Detailed Description Text (33):
In practicing the methods, DNA-dependent RNA polymerases and RNA-dependent RNA polymerases may be used. For example, RNA polymerases that may be used in the methods provided herein include, but are not limited to those obtained from: 1) archeabacteria, such as Halobacterium, Methanobacterium, Methanococcus, Sulfolobales and Thermoplasma; 2) eubacteria, such as gram negative bacteria, e.g., Escherichia coli and strains of Salmonella and Shigella, gram positive bacteria, e.g., Bacillus subtilis and Staphlococcus aureus; 3) bacteriophages, such as T7, T3, SP6 and N4; 4) DNA viruses; 5) RNA viruses, such as influenza virus; 6) plants and plant viruses, such as wheat and turnip mosiac virus; and 7) eukaryotic RNA polymerase II isolated from fungii, e.g., Saccharomvces cerevisae and higher eukaryotic organisms, e.g., mammals (e.g., for a review see In RNA Polymerase and the Regulation of Transcription, Rezinkoff et al., eds, Elsevier, N.Y.). Also included for use herein is the Q.beta. replicase from the Q.beta. RNA phage (e.g., see U.S. Pat. Nos. 5,670,353, 5,696,249 and Re: 35,443).

Detailed Description Text (35):
Each nucleic acid promoter-containing probe used in the sequencing methods described herein contains a promoter. The promoters used in the methods herein may be obtained from any source, i.e., recombinant or naturally-occurring promoter elements, or may be assembled from synthetic nucleic acid oligonucleotide sequences. For example, the nucleic acid containing a promoter may be obtained directly from a variety of different organisms, such as bacteria, viruses and eukaryotic organisms, by cloning or may be obtained from commercially available expression vectors (e.g., T7, T3, SP6 and .lambda..sub.PL and .lambda..sub.PR promoters; Boehringer Mannheim and Pharmacia; bla or lac promoters, RSV-LTR promoter and F9-1 promoter; Stratagene). The selection of the appropriate promoter will depend on the nucleic acid to be sequenced, sequencing conditions, and most importantly, on the RNA polymerase selected for transcription.

Detailed Description Text (64):
In practicing the methods described herein, a set of nested base-specific chain terminated RNA transcripts are generated during transcription by the incorporation of a modified base-specific chain terminating ribonucleotide analog. Any ribonucleoside triphosphate analog that results in the sequence-specific arrest of transcription elongation upon incorporation into an RNA molecule by an RNA polymerase may be used in the methods herein. Presently preferred ribonucleotide analogs are 3'-deoxyribonucleotides. The utilization of 3'-deoxyribonucleoside triphosphosphates by RNA polymerases has been reported to result in base-specific termination of transcription (e.g., see Axelrod et al. (1985) Biochemistry 24:5716-5723; Tyagarajan et al. (1985) Biochemistry 30:10920-10924).

Detailed Description Text (65):
In certain embodiments, in addition to a base-specific chain terminating ribonucleoside triphosphate analog, additional ribonucleotide analogs can be added to reduce the secondary structure of the resulting RNA transcript. For example, the incorporation of riboinosine using inosine 5'-triphosphate is known to reduce the secondary structure of RNA products. In the presence of a dinucleotide guanine initiator, inosine 5'-triphosphate can effectively substitute for GTP in in vitro transcription reactions (e.g., Axelrod et al. (1985) Biochemistry 24:5716-5723).

Detailed Description Text (66):
In addition, modified ribonucleotide analogs may be added to the transcription mixture to increase the efficiency of transcriptional termination and/or transcript release to promote and facilitate the rate enzyme turnover. For example, the addition of 4-thio UTP, 5-bromo UTP, 5-iodo CTP alter the hydrogen bonding of the nucleic acid facilitating, at least with some RNA polymerases, transcriptional termination and transcript release.

Detailed Description Text (111):
Transcription is initiated from the promoter by the addition of the appropriate RNA polymerase in the presence of ribonucleoside triphosphates under conditions described herein and known elsewhere (e.g., In RNA Polymerase and the Regulation of Transcription, Rezinkoff et al., eds, Elsevier, N.Y.). In preferred embodiments, a selected base-specific chain terminating 3'-deoxyribonucleoside triphosphate and the

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 3. Document ID: US 20020197623 A1

L16: Entry 3 of 75 File: PGPB Dec 26, 2002

PGPUB-DOCUMENT-NUMBER: 20020197623
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020197623 A1

TITLE: Nucleic acid detection assays

PUBLICATION-DATE: December 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Prudent, James R.	Madison	WI	US	
Hall, Jeff G.	Madison	WI	US	
Lyamichev, Victor I.	Madison	WI	US	
D. Brow, Mary Ann	Madison	WI	US	
Dahlberg, James E.			US	

US-CL-CURRENT: 435/6; 435/91.2, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 4. Document ID: US 20020197618 A1

L16: Entry 4 of 75 File: PGPB Dec 26, 2002

PGPUB-DOCUMENT-NUMBER: 20020197618
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020197618 A1

TITLE: Synthesis and amplification of unstructured nucleic acids for rapid sequencing

PUBLICATION-DATE: December 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Sampson, Jeffrey R.	Burlingame	CA	US	

US-CL-CURRENT: 435/6; 435/287.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 5. Document ID: US 20020193296 A1

L16: Entry 5 of 75 File: PGPB Dec 19, 2002

PGPUB-DOCUMENT-NUMBER: 20020193296
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020193296 A1

TITLE: Compositions and methods for the therapy and diagnosis of prostate cancer

PUBLICATION-DATE: December 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Xu, Jiangchun	Bellevue	WA	US	
Dillon, Davin C.	Issaquah	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Jiang, Yuqiu	Kent	WA	US	
Kalos, Michael D.	Seattle	WA	US	
Fanger, Gary R.	Mill Creek	WA	US	
Retter, Marc W.	Carnation	WA	US	
Stolk, John A.	Bothell	WA	US	
Day, Craig H.	Shoreline	WA	US	
Vedvick, Thomas S.	Federal Way	WA	US	
Carter, Darrick	Seattle	WA	US	
Li, Samuel X.	Redmond	WA	US	
Wang, Aijun	Issaquah	WA	US	
Skeiky, Yasir A. W.	Bellevue	WA	US	
Hepler, William T.	Seattle	WA	US	
Henderson, Robert A.	Edmonds	WA	US	
Hural, John	Bainbridge Island	WA	US	
McNeill, Patricia D.	Federal Way	WA	US	
Houghton, Raymond L.	Bothell	WA	US	
Bassols, Carlota Vinals y de	Rixensart	WA	BE	
Foy, Teresa M.	Federal Way		US	

US-CL-CURRENT: 514/12; 435/183, 435/320.1, 435/325, 435/6, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWMC | Draw Desc | Image

---

☐ 6. Document ID: US 20020192763 A1

L16: Entry 6 of 75 File: PGPB Dec 19, 2002

PGPUB-DOCUMENT-NUMBER: 20020192763
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020192763 A1

TITLE: Compositions and methods for the therapy and diagnosis of prostate cancer

PUBLICATION-DATE: December 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Xu, Jiangchun	Bellevue	WA	US	
Dillon, Davin C.	Issaquah	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Jiang, Yuqiu	Kent	WA	US	
Kalos, Michael D.	Seattle	WA	US	
Fanger, Gary R.	Mill Creek	WA	US	
Retter, Marc W.	Carnation	WA	US	
Stolk, John A.	Bothell	WA	US	
Day, Craig H.	Shoreline	WA	US	
Vedvick, Thomas S.	Federal Way	WA	US	
Carter, Darrick	Seattle	WA	US	
Li, Samuel X.	Redmond	WA	US	
Wang, Aijun	Issaquah	WA	US	
Skeiky, Yasir A. W.	Bellevue	WA	US	
Hepler, William T.	Seattle	WA	US	
Henderson, Robert A.	Edmonds	WA	US	
Hural, John	Bainbridge Island	WA	US	
McNeill, Patricia D.	Federal Way	WA	US	
Houghton, Raymond L.	Bothell	WA	US	
y de Bassols, Carlota Vinals	Rixensart	WA	BE	
Foy, Teresa M.	Federal Way		US	

US-CL-CURRENT: 435/69.7; 435/183, 435/320.1, 435/325, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 7. Document ID: US 20020187486 A1

L16: Entry 7 of 75 File: PGPB Dec 12, 2002

PGPUB-DOCUMENT-NUMBER: 20020187486
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020187486 A1

TITLE: Invasion assays

PUBLICATION-DATE: December 12, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hall, Jeff G.	Madison	WI	US	
Lyamichev, Victor I.	Madison	WI	US	
Mast, Andrea L.	Madison	WI	US	
Brow, Mary Ann D.	Madison	WI	US	

US-CL-CURRENT: 435/6; 435/91.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 8. Document ID: US 20020183499 A1

L16: Entry 8 of 75 File: PGPB Dec 5, 2002

PGPUB-DOCUMENT-NUMBER: 20020183499
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020183499 A1

TITLE: Compositions and methods for the therapy and diagnosis of lung cancer

PUBLICATION-DATE: December 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lodes, Michael J.	Seattle	WA	US	
Mohamath, Raodoh	Seattle	WA	US	
Henderson, Robert A.	Edmonds	WA	US	
Benson, Darin R.	Seattle	WA	US	
Secrist, Heather	Seattle	WA	US	

US-CL-CURRENT: 536/23.1; 424/184.1, 435/320.1, 435/325, 435/7.23, 530/324, 536/24.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 9. Document ID: US 20020183251 A1

L16: Entry 9 of 75 File: PGPB Dec 5, 2002

PGPUB-DOCUMENT-NUMBER: 20020183251
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020183251 A1

TITLE: Compositions and methods for the therapy and diagnosis of prostate cancer

PUBLICATION-DATE: December 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Xu, Jiangchun	Bellevue	WA	US	
Dillon, Davin C.	Issaquah	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Jiang, Yuqiu	Kent	WA	US	
Kalos, Michael D.	Seattle	WA	US	
Fanger, Gary R.	Mill Creek	WA	US	
Retter, Marc W.	Carnation	WA	US	
Stolk, John A.	Bothell	WA	US	
Day, Craig H.	Shoreline	WA	US	
Vedvick, Thomas S.	Federal Way	WA	US	
Carter, Darrick	Seattle	WA	US	
Li, Samuel X.	Redmond	WA	US	
Wang, Aijun	Issaquah	WA	US	
Skeiky, Yasir A.W.	Bellevue	WA	US	
Hepler, William T.	Seattle	WA	US	
Henderson, Robert A.	Edmonds	WA	US	
Hural, John	Bainbridge Island	WA	US	
McNeill, Patricia D.	Federal Way	WA	US	
Houghton, Raymond L.	Bothell	WA	US	
Vinals y de Bassols, Carlota	Rixensart	WA	BE	
Foy, Teresa M.	Federal Way	WA	US	
Watanabe, Yoshihiro	Mercer Island	WA	US	
Meagher, Madeleine Joy	Seattle		US	

US-CL-CURRENT: 514/12; 435/183, 435/320.1, 435/325, 435/6, 435/69.1, 530/350, 536/23.1

☐ 10. Document ID: US 20020177552 A1

L16: Entry 10 of 75 File: PGPB Nov 28, 2002

PGPUB-DOCUMENT-NUMBER: 20020177552
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020177552 A1

TITLE: Compositions and methods for the therapy and diagnosis of colon cancer

PUBLICATION-DATE: November 28, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Jiang, Yuqiu	Kent	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Secrist, Heather	Seattle	WA	US	

US-CL-CURRENT: 514/12; 435/183, 435/320.1, 435/325, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

Generate Collection | Print

Term	Documents
ANALOGUE.PGPB.	4330
ANALOG.PGPB.	29230
ANALOGS.PGPB.	7325
ANALOGUES.PGPB.	3450
(14 AND ANALOGUE).PGPB.	75
(L14 AND ANALOGUE).PGPB.	75

Display Format: CIT | Change Format

Previous Page Next Page

WEST

Generate Collection | Print

Search Results - Record(s) 21 through 30 of 75 returned.

☐ 21. Document ID: US 20020155473 A1

L16: Entry 21 of 75 File: PGPB Oct 24, 2002

PGPUB-DOCUMENT-NUMBER: 20020155473
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020155473 A1

TITLE: Methods for identifying G-protein coupled receptors associated with diseases

PUBLICATION-DATE: October 24, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Peng, Zaoyuan	Palo Alto	CA	US	
Yu, Zailin	San Leandro	CA	US	
Wiley, Andrew	Napa	CA	US	
Hu, Qianjin	Castro Valley	CA	US	

US-CL-CURRENT: 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 22. Document ID: US 20020150922 A1

L16: Entry 22 of 75 File: PGPB Oct 17, 2002

PGPUB-DOCUMENT-NUMBER: 20020150922
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020150922 A1

TITLE: Compositions and methods for the therapy and diagnosis of colon cancer

PUBLICATION-DATE: October 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Stolk, John A.	Bothell	WA	US	
Xu, Jiangchun	Bellevue	WA	US	
Chenault, Ruth A.	Seattle	WA	US	
Meagher, Madeleine Joy	Seattle	WA	US	

US-CL-CURRENT: 435/6; 435/183, 435/320.1, 435/325, 435/69.1, 435/7.23, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

---

☐ 23. Document ID: US 20020150581 A1

L16: Entry 23 of 75 File: PGPB Oct 17, 2002

PGPUB-DOCUMENT-NUMBER: 20020150581
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020150581 A1

TITLE: Compositions and methods for the therapy and diagnosis of breast cancer

PUBLICATION-DATE: October 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Jiang, Yuqiu	Kent	WA	US	
Dillon, Davin C.	Issaquah	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Xu, Jiangchun	Bellevue	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Hepler, William T.	Seattle	WA	US	
Henderson, Robert A.	Edmonds	WA	US	
Fanger, Gary R.	Mill Creek	WA	US	
Vedvick, Thomas S.	Federal Way	WA	US	
McNeill, Patricia D.	Federal Way	WA	US	
Durham, Margarita	Seattle	WA	US	

US-CL-CURRENT: 424/155.1; 435/183, 435/320.1, 435/325, 435/6, 435/69.1, 435/7.23, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

---

☐ 24. Document ID: US 20020147143 A1

L16: Entry 24 of 75 File: PGPB Oct 10, 2002

PGPUB-DOCUMENT-NUMBER: 20020147143
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020147143 A1

TITLE: Compositions and methods for the therapy and diagnosis of lung cancer

PUBLICATION-DATE: October 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Wang, Tongtong	Medina	WA	US	
Durham, Margarita	Seattle	WA	US	
Fanger, Gary R.	Mill Creek	WA	US	
Vedvick, Thomas S.	Federal Way	WA	US	
Carter, Darrick	Seattle	WA	US	
Watanabe, Yoshihiro	Mercer Island	WA	US	
Henderson, Robert A.	Edmonds	WA	US	
Peckham, David W.	Seattle	WA	US	
Fanger, Neil	Seattle	WA	US	

US-CL-CURRENT: 514/12; 435/183, 435/320.1, 435/325, 435/69.1, 514/44, 530/350, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 25. Document ID: US 20020146776 A1

L16: Entry 25 of 75 File: PGPB Oct 10, 2002

PGPUB-DOCUMENT-NUMBER: 20020146776
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020146776 A1

TITLE: Compounds and methods for treatment and diagnosis of chlamydial infection

PUBLICATION-DATE: October 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bhatia, Ajay	Seattle	WA	US	
Probst, Peter	Seattle	WA	US	

US-CL-CURRENT: 435/69.3; 435/183, 435/252.3, 435/320.1, 536/23.7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 26. Document ID: US 20020146727 A1

L16: Entry 26 of 75 File: PGPB Oct 10, 2002

PGPUB-DOCUMENT-NUMBER: 20020146727
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020146727 A1

TITLE: Compositions and methods for the therapy and diagnosis of breast cancer

PUBLICATION-DATE: October 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Dillon, Davin C.	Issaquah	WA	US	
Day, Craig H.	Shoreline	WA	US	
Jiang, Yuqiu	Kent	WA	US	
Houghton, Raymond L.	Bothell	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Wang, Tongtong	Medina	WA	US	
McNeill, Patricia D.	Federal Way	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Bennigton, Angela Ann	Seattle	WA	US	
Zehentner, Barbara	Bainbridge Island	WA	US	
Fanger, Gary R.	Mill Creek	WA	US	
Retter, Marc W.	Carnation	WA	US	

US-CL-CURRENT: 435/6; 435/183, 435/320.1, 435/325, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 27. Document ID: US 20020146717 A1

L16: Entry 27 of 75 File: PGPB Oct 10, 2002

PGPUB-DOCUMENT-NUMBER: 20020146717
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020146717 A1

TITLE: Compositions, methods and kits for determining the presence of cryptosporidium parvum organisms in a test sample

PUBLICATION-DATE: October 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Cunningham, Melissa M.	Gresham	OR	US	
Stull, Paul D.	San Diego	CA	US	
Weisburg, William G.	San Diego	CA	US	

US-CL-CURRENT: 435/6; 536/23.7, 536/24.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 28. Document ID: US 20020142957 A1

L16: Entry 28 of 75 File: PGPB Oct 3, 2002

PGPUB-DOCUMENT-NUMBER: 20020142957
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020142957 A1

TITLE: Compositions and methods for the therapy and diagnosis of colon cancer

PUBLICATION-DATE: October 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hepler, William T.	Seattle	WA	US	
Jiang, Yuqiu	Kent	WA	US	
Pyle, Ruth A.	Seattle	WA	US	
Xu, Jiangchun	Bellevue	WA	US	

US-CL-CURRENT: 514/12; 435/320.1, 435/325, 435/69.3, 435/7.23, 514/44, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 29. Document ID: US 20020137911 A1

L16: Entry 29 of 75 File: PGPB Sep 26, 2002

PGPUB-DOCUMENT-NUMBER: 20020137911
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020137911 A1

TITLE: Compositions and methods for the therapy and diagnosis of pancreatic cancer

PUBLICATION-DATE: September 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Pyle, Ruth A.	Seattle	WA	US	
Xu, Jiangchun	Bellevue	WA	US	

US-CL-CURRENT: 536/23.2; 435/183, 435/320.1, 435/325, 435/69.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 30. Document ID: US 20020137709 A1

L16: Entry 30 of 75 File: PGPB Sep 26, 2002

PGPUB-DOCUMENT-NUMBER: 20020137709
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020137709 A1

TITLE: Gene silencing using mRNA-cDNA hybrids

PUBLICATION-DATE: September 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lin, Shi-Lung	Alhambra	CA	US	
Chuong, Cheng-Ming	Irvine	CA	US	
Widelitz, Randall B.	Fullerton	CA	US	

US-CL-CURRENT: 514/44; 435/91.2, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

Generate Collection | Print

Term	Documents
ANALOGUE.PGPB.	4330
ANALOG.PGPB.	29230
ANALOGS.PGPB.	7325
ANALOGUES.PGPB.	3450
(14 AND ANALOGUE).PGPB.	75
(L14 AND ANALOGUE).PGPB.	75

Display Format: CIT | Change Format

Previous Page Next Page

WEST

Generate Collection | Print

Search Results - Record(s) 41 through 50 of 75 returned.

☐ 41. Document ID: US 20020102567 A1

L16: Entry 41 of 75 File: PGPB Aug 1, 2002

PGPUB-DOCUMENT-NUMBER: 20020102567
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020102567 A1

TITLE: Method for comparing nucleic acid sequences

PUBLICATION-DATE: August 1, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Fodor, Stephen P.A.	Palo Alto	CA	US	
Solas, Dennis W.	San Francisco	CA	US	
Dower, William J.	Menlo Park	CA	US	

US-CL-CURRENT: 435/6; 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 42. Document ID: US 20020102267 A1

L16: Entry 42 of 75 File: PGPB Aug 1, 2002

PGPUB-DOCUMENT-NUMBER: 20020102267
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020102267 A1

TITLE: CLASP-5 transmembrane protein

PUBLICATION-DATE: August 1, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lu, Peter S.	Mountain View	CA	US	
Garman, Jonathan D.	San Jose	CA	US	
Candia, Albert F. III	Menlo Park	CA	US	

US-CL-CURRENT: 424/185.1; 435/320.1, 435/325, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 43. Document ID: US 20020099012 A1

L16: Entry 43 of 75 File: PGPB Jul 25, 2002

PGPUB-DOCUMENT-NUMBER: 20020099012
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020099012 A1

TITLE: Compositions and methods for the therapy and diagnosis of lung cancer

PUBLICATION-DATE: July 25, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Wang, Tongtong	Medina	WA	US	
McNeill, Patricia D.	Federal Way	WA	US	
Watanabe, Yoshihiro	Mercer Island	WA	US	
Carter, Darrick	Seattle	WA	US	
Henderson, Robert A.	Edmonds	WA	US	
Kalos, Michael D.	Seattle	WA	US	

US-CL-CURRENT: 514/12; 435/183, 435/320.1, 435/325, 435/6, 435/69.1, 530/350, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

---

☐ 44. Document ID: US 20020090610 A1

L16: Entry 44 of 75 File: PGPB Jul 11, 2002

PGPUB-DOCUMENT-NUMBER: 20020090610
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020090610 A1

TITLE: Compositions and methods for the diagnosis and treatment of herpes simplex virus infection

PUBLICATION-DATE: July 11, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hosken, Nancy A.	Seattle	WA	US	
Day, Craig H.	Seattle	WA	US	
Dillon, Davin C.	Issaquah	WA	US	
McGowan, Patrick	Seattle	WA	US	
Sleath, Paul R.	Seattle	WA	US	

US-CL-CURRENT: 435/5; 424/231.1, 435/6, 530/350, 536/23.72

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

---

☐ 45. Document ID: US 20020086382 A1

L16: Entry 45 of 75 File: PGPB Jul 4, 2002

PGPUB-DOCUMENT-NUMBER: 20020086382
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020086382 A1

TITLE: Clasp-3 transmembrane protein

PUBLICATION-DATE: July 4, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lu, Peter S.	Mountain View	CA	US	
Garman, Jonathan D.	San Jose	CA	US	
Candia, Albert F. III	Menlo Park	CA	US	

US-CL-CURRENT: 435/183; 435/320.1, 435/325, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 46. Document ID: US 20020086303 A1

L16: Entry 46 of 75 File: PGPB Jul 4, 2002

PGPUB-DOCUMENT-NUMBER: 20020086303
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020086303 A1

TITLE: Compositions and methods for the therapy and diagnosis of colon cancer

PUBLICATION-DATE: July 4, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Meagher, Madeleine Joy	Seattle	WA	US	
King, Gordon E.	Shoreline	WA	US	
Xu, Jiangchun	Bellevue	WA	US	
Secrist, Heather	Seattle	WA	US	

US-CL-CURRENT: 435/6; 424/155.1, 435/183, 435/320.1, 435/325, 435/69.1, 435/7.23, 514/44, 530/388.8, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 47. Document ID: US 20020085998 A1

L16: Entry 47 of 75 File: PGPB Jul 4, 2002

PGPUB-DOCUMENT-NUMBER: 20020085998
PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020085998 A1

TITLE: Compositions and methods for the therapy and diagnosis of breast cancer

PUBLICATION-DATE: July 4, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Jiang, Yuqiu	Kent	WA	US	
Dillon, Davin C.	Issaquah	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Xu, Jiangchun	Bellevue	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Hepler, William T.	Seattle	WA	US	
Henderson, Robert A.	Edmonds	WA	US	

US-CL-CURRENT: 424/93.21; 435/183, 435/320.1, 435/325, 435/69.1, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

---

☐ 48. Document ID: US 20020082207 A1

L16: Entry 48 of 75 File: PGPB Jun 27, 2002

PGPUB-DOCUMENT-NUMBER: 20020082207
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020082207 A1

TITLE: Compositions and methods for the therapy and diagnosis of pancreatic cancer

PUBLICATION-DATE: June 27, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hirst, Shannon K.	Kirkland	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Dillon, Davin C.	Issaquah	WA	US	
Kalos, Michael D.	Seattle	WA	US	

US-CL-CURRENT: 514/12; 435/183, 435/320.1, 435/325, 435/6, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

---

☐ 49. Document ID: US 20020081680 A1

L16: Entry 49 of 75 File: PGPB Jun 27, 2002

PGPUB-DOCUMENT-NUMBER: 20020081680
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020081680 A1

TITLE: Compositions and methods for the therapy and diagnosis of prostate cancer

PUBLICATION-DATE: June 27, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Xu, Jiangchun	Bellevue	WA	US	
Dillon, Davin C.	Issaquah	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Jiang, Yuqiu	Kent	WA	US	
Kalos, Michael D.	Seattle	WA	US	
Fanger, Gary R.	Mill Creek	WA	US	
Retter, Marc W.	Carnation	WA	US	
Stolk, John A.	Bothell	WA	US	
Day, Craig H.	Seattle	WA	US	
Vedvick, Thomas S.	Federal Way	WA	US	
Carter, Darrick	Seattle	WA	US	
Li, Samuel X.	Redmond	WA	US	
Wang, Aijun	Issaquah	WA	US	
Skeiky, Yasir A. W.	Bellevue	WA	US	
Hepler, William T.	Seattle	WA	US	
Henderson, Robert A.	Edmonds	WA	US	
Hural, John	Bainbridge Island	WA	US	
McNeill, Patricia D.	Federal Way	WA	US	
Houghton, Raymond L.	Bothell	WA	US	
de Bassols, Carlota Vinals	Rixensart		BE	

US-CL-CURRENT: 435/183; 435/320.1, 435/325, 435/69.7, 530/350, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

---

☐ 50. Document ID: US 20020081609 A1

L16: Entry 50 of 75 File: PGPB Jun 27, 2002

PGPUB-DOCUMENT-NUMBER: 20020081609
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020081609 A1

TITLE: Compositions and methods for the therapy and diagnosis of breast cancer

PUBLICATION-DATE: June 27, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Dillon, Davin C.	Issaquah	WA	US	
Day, Craig H.	Shoreline	WA	US	
Jiang, Yuqiu	Kent	WA	US	
Houghton, Raymond L.	Bothell	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Wang, Tongtong	Medina	WA	US	
McNeill, Patricia D.	Federal Way	WA	US	
Harlocker, Susan L.	Seattle	WA	US	

US-CL-CURRENT: 435/6; 435/183, 435/320.1, 435/325, 435/69.1, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

Generate Collection | Print

Term	Documents
ANALOGUE.PGPB.	4330
ANALOG.PGPB.	29230
ANALOGS.PGPB.	7325
ANALOGUES.PGPB.	3450
(14 AND ANALOGUE).PGPB.	75
(L14 AND ANALOGUE).PGPB.	75

Display Format: CIT | Change Format

Previous Page Next Page

WEST

Generate Collection | Print

Search Results - Record(s) 51 through 60 of 75 returned.

☐ 51. Document ID: US 20020076721 A1

L16: Entry 51 of 75 File: PGPB Jun 20, 2002

PGPUB-DOCUMENT-NUMBER: 20020076721
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020076721 A1

TITLE: Compositions and methods for the therapy and diagnosis of pancreatic cancer

PUBLICATION-DATE: June 20, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Pyle, Ruth A.	Seattle	WA	US	
Xu, Jiangchun	Bellevue	WA	US	
Kalos, Michael D.	Seattle	WA	US	

US-CL-CURRENT: 435/6; 435/183, 435/320.1, 435/325, 435/69.3, 435/7.23, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 52. Document ID: US 20020072503 A1

L16: Entry 52 of 75 File: PGPB Jun 13, 2002

PGPUB-DOCUMENT-NUMBER: 20020072503
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020072503 A1

TITLE: Compositions and methods for the therapy and diagnosis of ovarian cancer

PUBLICATION-DATE: June 13, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Xu, Jiangchun	Bellevue	WA	US	
Stolk, John A.	Bothell	WA	US	

US-CL-CURRENT: 514/44; 424/277.1, 424/93.21

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 53. Document ID: US 20020068302 A1

L16: Entry 53 of 75 File: PGPB Jun 6, 2002

PGPUB-DOCUMENT-NUMBER: 20020068302
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020068302 A1

TITLE: Clasp-4 transmembrane protein

PUBLICATION-DATE: June 6, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lu, Peter S.	Mountain View	CA	US	
Garman, Jonathan D.	San Jose	CA	US	
Candia, Albert F. III	Menlo Park	CA	US	

US-CL-CURRENT: 435/7.1; 530/350, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

---

☐ 54. Document ID: US 20020068288 A1

L16: Entry 54 of 75 File: PGPB Jun 6, 2002

PGPUB-DOCUMENT-NUMBER: 20020068288
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020068288 A1

TITLE: Compositions and methods for the therapy and diagnosis of lung cancer

PUBLICATION-DATE: June 6, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lodes, Michael J.	Seattle	WA	US	
Wang, Tongtong	Medina	WA	US	
Mohamath, Raodoh	Seattle	WA	US	
Indirias, Carol Yoseph	Seattle	WA	US	

US-CL-CURRENT: 435/6; 435/183, 435/320.1, 435/325, 435/69.1, 435/7.23, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

---

☐ 55. Document ID: US 20020068285 A1

L16: Entry 55 of 75 File: PGPB Jun 6, 2002

PGPUB-DOCUMENT-NUMBER: 20020068285
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020068285 A1

TITLE: Compositions and methods for the therapy and diagnosis of breast cancer

PUBLICATION-DATE: June 6, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Frudakis, Tony N.	Sarasota	FL	US	
Reed, Steven G.	Bellevue	WA	US	
Smith, John M.	Columbia Heights	MN	US	
Misher, Lynda E.	Seattle	WA	US	
Dillon, Davin C.	Issaquah	WA	US	
Retter, Marc W.	Carnation	WA	US	
Wang, Aijun	Issaquah	WA	US	
Skeiky, Yasir A. W.	Bellevue	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Day, Craig H.	Seattle	WA	US	

US-CL-CURRENT: 435/6; 435/325, 435/69.7, 435/7.23, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

---

☐ 56. Document ID: US 20020064872 A1

L16: Entry 56 of 75 File: PGPB May 30, 2002

PGPUB-DOCUMENT-NUMBER: 20020064872
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020064872 A1

TITLE: Compositions and methods for the therapy and diagnosis of breast cancer

PUBLICATION-DATE: May 30, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Jiang, Yuqui	Kent	WA	US	
Dillon, Davin C.	Isaaquah	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Xu, Jiangchun	Bellevue	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Hepler, William T.	Seattle	WA	US	

US-CL-CURRENT: 435/325; 424/130.1, 424/93.1, 435/7.1, 514/2, 514/44, 530/350, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

---

☐ 57. Document ID: US 20020064824 A1

L16: Entry 57 of 75 File: PGPB May 30, 2002

PGPUB-DOCUMENT-NUMBER: 20020064824
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020064824 A1

TITLE: Screening system for zinc finger polypeptides for a desired binding ability

PUBLICATION-DATE: May 30, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Choo, Yen	Cambridge		GB	
Moore, Michael	Amersham Bucks		GB	

US-CL-CURRENT: 435/69.1; 435/320.1, 435/91.21, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 58. Document ID: US 20020055116 A1

L16: Entry 58 of 75 File: PGPB May 9, 2002

PGPUB-DOCUMENT-NUMBER: 20020055116
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020055116 A1

TITLE: Compositions, methods and kits for determining the presence of cryptosporidium organisms in a test sample

PUBLICATION-DATE: May 9, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Cunningham, Melissa M.	Gresham	OR	US	
Stull, Paul D.	San Diego	CA	US	
Weisburg, William G.	San Diego	CA	US	

US-CL-CURRENT: 435/6; 536/24.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 59. Document ID: US 20020052329 A1

L16: Entry 59 of 75 File: PGPB May 2, 2002

PGPUB-DOCUMENT-NUMBER: 20020052329
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020052329 A1

TITLE: Compositions and methods for the therapy and diagnosis of lung cancer

PUBLICATION-DATE: May 2, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Wang, Tongtong	Medina	WA	US	
Fan, Liqun	Bellevue	WA	US	
Kalos, Michael D.	Seattle	WA	US	
Bangur, Chaitanya S.	Seattle	WA	US	
Hosken, Nancy A.	Seattle	WA	US	
Fanger, Gary R.	Mill Creek	WA	US	
Li, Samuel X.	Redmond	WA	US	
Wang, Aijun	Issaquah	WA	US	
Skeiky, Yasir A. W.	Bellevue	WA	US	
Henderson, Robert A.	Edmonds	WA	US	
McNeill, Patricia D.	Des Moines	WA	US	
Fanger, Neil	Seattle	WA	US	

US-CL-CURRENT: 514/44; 435/183, 435/320.1, 435/325, 435/6, 435/7.23, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

---

☐ 60. Document ID: US 20020051977 A1

L16: Entry 60 of 75 File: PGPB May 2, 2002

PGPUB-DOCUMENT-NUMBER: 20020051977
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020051977 A1

TITLE: Compositions and methods for the therapy and diagnosis of prostate cancer

PUBLICATION-DATE: May 2, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Xu, Jiangchun	Bellevue	WA	US	
Dillon, Davin C.	Issaquah	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Harlocker, Susan L.	Seattle	WA	US	
Jiang, Yuqiu	Kent	WA	US	
Kalos, Michael D.	Seattle	WA	US	
Fanger, Gary R.	Mill Creek	WA	US	
Retter, Marc W.	Carnation	WA	US	
Stolk, John A.	Bothell	WA	US	
Day, Craig H.	Seattle	WA	US	
Vedvick, Thomas S.	Federal Way	WA	US	
Carter, Darrick	Seattle	WA	US	
Li, Samuel X.	Redmond	WA	US	
Wang, Aijun	Issaquah	WA	US	
Skeiky, Yasir A. W.	Bellevue	WA	US	
Hepler, William T.	Seattle	WA	US	
Henderson, Robert A.	Edmonds	WA	US	
Hural, John	Bainbridge Island	WA	US	
McNeill, Patricia D.	Des Moines	WA	US	
Houghton, Raymond L.	Bothell	WA	US	

US-CL-CURRENT: 435/6; 424/184.1, 424/93.21, 435/69.3, 435/7.23, 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

Generate Collection | Print

Term	Documents
ANALOGUE.PGPB.	4330
ANALOG.PGPB.	29230
ANALOGS.PGPB.	7325
ANALOGUES.PGPB.	3450
(14 AND ANALOGUE).PGPB.	75
(L14 AND ANALOGUE).PGPB.	75

Display Format: CIT | Change Format

Previous Page Next Page

WEST

Generate Collection | Print

Search Results - Record(s) 71 through 75 of 75 returned.

☐ 71. Document ID: US 20020004491 A1

L16: Entry 71 of 75 File: PGPB Jan 10, 2002

PGPUB-DOCUMENT-NUMBER: 20020004491
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020004491 A1

TITLE: Compositions and methods for the therapy and diagnosis of ovarian cancer

PUBLICATION-DATE: January 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Xu, Jiangchun	Bellevue	WA	US	
Stolk, John A.	Bothell	WA	US	
Algate, Paul A.	Issaquah	WA	US	
Fling, Steven P.	Bainbridge Island	WA	US	

US-CL-CURRENT: 514/44; 424/155.1, 435/183, 435/325, 435/69.1, 514/12, 530/350, 530/387.1, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

☐ 72. Document ID: US 20010053519 A1

L16: Entry 72 of 75 File: PGPB Dec 20, 2001

PGPUB-DOCUMENT-NUMBER: 20010053519
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010053519 A1

TITLE: Oligonucleotides

PUBLICATION-DATE: December 20, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Fodor, Stephen P.A.	Palo Alto	CA	US	
Solas, Dennis W.	San Francisco	CA	US	
Dower, William J.	Menlo Park	CA	US	
Huang, Xiaohua C.	Mountain View	CA	US	

US-CL-CURRENT: 435/6; 435/3, 536/24.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC
Draw Desc | Image

☐ 73. Document ID: US 20010044105 A1

L16: Entry 73 of 75 File: PGPB Nov 22, 2001

PGPUB-DOCUMENT-NUMBER: 20010044105
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010044105 A1

TITLE: Process for labeling a ribonucleic acid, and labeled RNA fragments which are obtained thereby

PUBLICATION-DATE: November 22, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Laayoun, Ali	Lyon	CA	FR	
Do, Duc	San Jose	CA	US	
Miyada, Charles G.	San Jose		US	

US-CL-CURRENT: 435/6; 435/91.1, 536/25.32

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWMC
Draw Desc | Image

☐ 74. Document ID: US 20010034052 A1

L16: Entry 74 of 75 File: PGPB Oct 25, 2001

PGPUB-DOCUMENT-NUMBER: 20010034052
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010034052 A1

TITLE: Compositions and methods for the therapy and diagnosis of breast cancer

PUBLICATION-DATE: October 25, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Dillon, Davin C.	Issaquah	WA	US	
Day, Craig H.	Seattle	WA	US	
Jiang, Yuqiu	Kent	WA	US	
Houghton, Raymond L.	Bothell	WA	US	
Mitcham, Jennifer L.	Redmond	WA	US	
Wang, Tongtong	Medina	WA	US	
McNeill, Patricia D.	Des Moines	WA	US	

US-CL-CURRENT: 435/200; 435/6, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWMC
Draw Desc | Image

☐ 75. Document ID: US 20010034048 A1

L16: Entry 75 of 75 File: PGPB Oct 25, 2001

PGPUB-DOCUMENT-NUMBER: 20010034048
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010034048 A1

TITLE: Methods and compositions for linear isothermal amplification of polynucleotide sequences

PUBLICATION-DATE: October 25, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kurn, Nurith	Palo Alto	CA	US	

US-CL-CURRENT: 435/91.1; 435/91.2, 536/24.33

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

Generate Collection Print

Term	Documents
ANALOGUE.PGPB.	4330
ANALOG.PGPB.	29230
ANALOGS.PGPB.	7325
ANALOGUES.PGPB.	3450
(14 AND ANALOGUE).PGPB.	75
(L14 AND ANALOGUE).PGPB.	75

Display Format: CIT Change Format

Previous Page Next Page

WEST

End of Result Set

☐ Generate Collection Print

L16: Entry 75 of 75 File: PGPB Oct 25, 2001

DOCUMENT-IDENTIFIER: US 20010034048 A1
TITLE: Methods and compositions for linear isothermal amplification of polynucleotide sequences

Summary of Invention Paragraph (10):
[0010] Target nucleic acid amplification may be carried out through multiple cycles of incubations at various temperatures, i.e. thermal cycling, or at one temperature (an isothermal process). The discovery of thermostable nucleic acid modifying enzymes has contributed to the fast advances in nucleic acid amplification technology. See Saiki, et al. Science 239:487 (1988). Thermostable nucleic acid modifying enzymes, such as DNA and RNA polymerases, ligases, nucleases and the like, are used in both methods dependent on thermal cycling and isothermal amplification methods. Isothermal methods such as strand displacement amplification (SDA) is disclosed by Fraiser et al. in U.S. Pat. No. 5,648,211; Cleuziat et al. in U.S. Pat. No. 5,824,517; and Walker et al. Proc. Natl. Acad. Sci. U.S.A. 89:392-396 (1992). Other isothermal target amplification methods are the transcription-based amplification methods, in which an RNA polymerase promoter sequence is incorporated into primer extension products at an early stage of the amplification (WO 89/01050), and further target sequence, or target complementary sequence, is amplified by transcription steps and digestion of an RNA strand in a DNA/RNA hybrid intermediate product. See, for example, U.S. Pat. Nos. 5,169,766 and 4,786,600. These methods include transcription mediated amplification (TMA), self-sustained sequence replication (3SR), Nucleic Acid Sequence Based Amplification (NASBA), and variations there of. See, for example, Guatelli et al. Proc. Natl. Acad. Sci. U.S.A. 87:1874-1878 (1990); U.S. Pat. Nos. 5,766,849 (TMA); and 5,654,142 (NASBA). Other amplifications methods use template switching oligonucleotides (TSOs) and blocking oligonucleotides. For example, the template switch amplification in which chimeric DNA primer are utilitized is disclosed in U.S. Pat. No. 5,679,512 and by Patel et al. Proc. Natl. Acad. Sci. U.S.A. 93:2969-2974 (1996) and blocking oligonucleotides are disclosed by Laney et al. in U.S. Pat. No. 5,679,512.

Summary of Invention Paragraph (19):
[0018] In another aspect, the invention provides methods for amplifying a target polynucleotide sequence comprising: (a) hybridizing a single stranded DNA template comprising the target sequence with a composite primer, said composite primer comprising an RNA portion and a 3' DNA portion; (b) hybridizing a polynucleotide comprising a termination polynucleotide sequence to a region of the template which is 5' with respect hybridization of the composite primer to the template; (c) extending the composite primer with DNA polyrnerase; (d) cleaving the RNA portion of the annealed composite primer with an enzyme that cleaves RNA from an RNA/DNA hybrid such that another composite primer can hybridize to the template and repeat primer extension by strand displacement to produce displaced primer extension product; (e) hybridizing a polynucleotide comprising a propromoter and a region which hybridizes to the displaced primer extension product under conditions which allow transcription to occur by RNA polymerase, such that RNA transcripts are produced comprising sequences complementary to the displaced primer extension products, whereby multiple copies of the target sequence are produced.

Summary of Invention Paragraph (26):
[0025] Accordingly, in one aspect, the invention provides methods of sequencing a target nucleotide sequence comprising: (a) hybridizing a single stranded DNA

template comprising the target sequence with a composite primer, said composite primer comprising an RNA portion and a 3' DNA portion; (b) optionally hybridizing a polynucleotide comprising a termination polynucleotide sequence to a region of the template which is 5' with respect hybridization of the composite primer to the template; (c) extending the composite primer with DNA polymerase and a mixture of dNTPs and dNTP analogs (which may be labelled or unlabelled), such that primer extension is terminated upon incorporation of a dNTP analog which may be labelled or unlabelled; (d) cleaving the RNA portion of the annealed composite primer with an enzyme that cleaves RNA from an RNA/DNA hybrid such that another composite primer can hybridize to the template and repeat primer extension by strand displacement, whereby multiple copies of the complementary sequence of the target sequence are produced of varying lengths; (e) analyzing the product of steps (a) through (d) to determine sequence.

Summary of Invention Paragraph (27):
[0026] In another aspect, the invention provides methods for sequencing a target nucleotide sequence comprising (a) hybridizing a single stranded DNA template comprising the target sequence with a composite primer, said composite primer comprising an RNA portion and a 3' DNA portion; (b) hybridizing the template with a polynucleotide comprising a termination polynucleotide sequence to a region of the template which is 5' with respect to hybridization of the composite primer to the template; (c) extending the composite primer with DNA polymerase; (d) cleaving the RNA portion of the annealed composite primer with an enzyme that cleaves RNA from an RNA/DNA hybrid such that another composite primer can hybridize to the template and repeat primer extension by strand displacement to produce displaced primer extension product; (e) hybridizing a polynucleotide comprising a propromoter at the 5' end and a region which hybridizes to the displaced primer extension product under conditions such that transcription occurs from the extension product by RNA polymerase, using a mixture of rNTPs and rNTP analogs (which may be labelled or unlabelled), such that RNA transcripts are produced comprising sequences complementary to the displaced primer extension products, and such that transcription is terminated upon incorporation of an rNTP analog which may be labelled or unlabelled, whereby multiple copies of the target sequence are produced of varying lengths; (f) analyzing the product of steps (a) through (e) to determine sequence.

Summary of Invention Paragraph (35):
[0034] In another aspect, the invention provides reaction mixtures (or compositions comprising reaction mixtures) which contain various combinations of components described herein. For example, the invention provides reaction mixtures comprising (a) a polynucleotide template; (b) a composite primer comprising a 3' DNA portion and an RNA portion; and (c) DNA polymerase. As described herein, any of the composite primers may be in the reaction mixture (or a plurality of composite primers), including a composite primer comprises a 5' RNA portion which is adjacent to the 3' DNA portion. The reaction mixture could also further comprise an enzyme which cleaves RNA from an RNA/DNA hybrid, such as RNase H. A reaction mixture of the invention can also comprise any of the polynucleotides comprising termination sequences described herein, as well as a polynucleotide comprising a propromoter and a region which hybridizes to displaced primer extension product, and an RNA polymerase. A reaction mixture of the invention can also comprise a PTO.

Detail Description Paragraph (3):
[0048] As a general summary, the amplification methods work as follows: a composite RNA/DNA primer forms the basis for replication of target sequence. In some embodiments, a termination sequence provides the basis for an endpoint for the replication by either diverting or blocking further replication along the target strand. As described below, in some embodiments, the polynucleotide comprising a termination sequence is a template switch oligonucleotide (TSO), which contains sequences that are not of sufficient complementarity to hybridize to the template strand (in addition to sequences which are of sufficient complementary to hybridize); in other embodiments, the termination sequence comprises primarily sequences that are of sufficient complementarity to hybridize to the template strand. DNA polymerase effects copying of the target sequence from the primer. An enzyme which cleaves RNA from an RNA/DNA hybrid (such as RNaseH) cleaves (removes) RNA sequence from the hybrid, leaving sequence on the template strand available for binding by another composite primer. Another strand is produced by DNA polymerase,

which displaces the previously replicated strand, resulting in displaced extension product. Optionally, a polynucleotide comprising a propromoter and a region which hybridizes to the displaced primer extension product (which can be, for example, a template switch oligonucleotide or propromoter template oligonucleotide), which contains sequences of sufficient complementarity to hybridize to the 3' end of the displacement extension product, binds to the displaced primer extension product. The promoter drives transcription (via DNA-dependent RNA polymerase) to produce sense RNA products.

Detail Description Paragraph (4):
[0049] Accordingly, the invention provides methods of producing at least one copy of a target polynucleotide sequence (generally, methods of amplifying target polynucleotide sequence) comprising combining and reacting the following: (a) a single-stranded target polynucleotide comprising a target sequence; (b) a composite primer comprising an RNA portion and a 3' DNA portion; (c) a DNA polymerase; (d) deoxyribonucleoside triphosphates or suitable analogs; (e) an enyzme, such as RNaseH, which cleaves RNA from an RNA/DNA duplex; and (f) generally, but optionally, a polynucleotide comprising a termination sequence, such as any of those described herein, which comprises a portion (or region) which hybridizes to the template polynucleotide. A termination sequence is used if transcription-based amplification (see below) is also used. The combination is subjected to suitable conditions such that (a) the composite primer (and, optionally, a polynucleotide comprising a termination sequence) hybridizes to the template; (b) primer extension occurs from the composite primer, to form a duplex; (c) RNaseH cleaves RNA of the composite primer from the RNA/DNA duplex; (d) another composite primer hybridizes to the template, and another round of primer extension (mediated by DNA polymerase) occurs, displacing the strand already copied from the template.

Detail Description Paragraph (5):
[0050] Optionally, the following is also included in the amplification reaction (either at the same time as those components listed above or added separately): (e) a polynucleotide comprising a propromoter sequence (which can be in any of a number of forms, as described herein) and a region which hybridizes to the displaced primer extension product; (f) ribonucleoside triphosphates or suitable analogs; and (g) RNA polymerase, under conditions such that transcription of the displaced strand can occur. Details regarding the various components of the methods of the present invention are provided below.

Detail Description Paragraph (6):
[0051] In some embodiments, the invention provides methods of sequencing nucleic acids (DNA or RNA). For the sequencing methods, the appropriate dNTPs (or, when embodiments which rely on transcription-based amplifications are used, appropriate rNTPs), which may be labelled or unlabelled, are used. Accordingly, the invention provides methods of sequencing a target nucleotide sequence comprising the methods described above, wherein dNTPs and dNTP analogs which are primer elongation terminators, which may be labelled or unlabelled, and/or rNTPs and rNTP analogs, which are primer elongation terminators, which may be labelled or unlabelled, are used, and the amplification product is analyzed for sequence information, as described below.

Detail Description Paragraph (24):
[0069] "Amplification," as used herein, generally refers to the process of producing multiple copies of a desired sequence. "Multiple copies" mean at least 2 copies. A "copy" does not necessarily mean perfect sequence complementarity or identity to the template sequence. For example, copies can include nucleotide analogs such as deoxyinosine, intentional sequence alterations (such as sequence alterations introduced through a primer comprising a sequence that is hybridizable, but not complementary, to the template), and/or sequence errors that occur during amplification.

Detail Description Paragraph (25):
[0070] "Polynucleotide," or "nucleic acid," as used interchangeably herein, refer to polymers of nucleotides of any length, and include DNA and RNA. The nucleotides can be deoxyribonucleotides, ribonucleotides, modified nucleotides or bases, and/or their analogs, or any substrate that can be incorporated into a polymer by DNA or

RNA polymerase. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and their analogs. If present, modification to the nucleotide structure may be imparted before or after assembly of the polymer. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. Other types of modifications include, for example, "caps", substitution of one or more of the naturally occurring nucleotides with an analog, intemucleotide modifications such as, for example, those with uncharged linkages (e.g., methyl phosphonates, phosphotriesters, phosphoamidates, cabamates, etc.) and with charged linkages (e.g., phosphorothioates, phosphorodithioates, etc.), those containing pendant moieties, such as, for example, proteins (e.g., nucleases, toxins, antibodies, signal peptides, ply-L-lysine, etc.), those with intercalators (e.g., acridine, psoralen, etc.), those containing chelators (e.g., metals, radioactive metals, boron, oxidative metals, etc.), those containing alkylators, those with modified linkages (e.g., alpha anomeric nucleic acids, etc.), as well as unmodified forms of the polynucleotide(s). Further, any of the hydroxyl groups ordinarily present in the sugars may be replaced, for example, by phosphonate groups, phosphate groups, protected by standard protecting groups, or activated to prepare additional linkages to additional nucleotides, or may be conjugated to solid supports. The 5' and 3' terminal OH can be phosphorylated or substituted with amines or organic capping groups moieties of from 1 to 20 carbon atoms. Other hydroxyls may also be derivatized to standard protecting groups. Polynucleotides can also contain analogous forms of ribose or deoxyribose sugars that are generally known in the art, including, for example, 2'--O-methyl-, 2'-O-allyl, 2'-fluoro- or 2'-azido-ribose, carbocyclic sugar analogs, .alpha.-anomeric sugars, epimeric sugars such as arabinose, xyloses or lyxoses, pyranose sugars, furanose sugars, sedoheptuloses, acyclic analogs and abasic nucleoside analogs such as methyl riboside. One or more phosphodiester linkages may be replaced by alternative linking groups. These alternative linking groups include, but are not limited to, embodiments wherein phosphate is replaced by P(O)S("thioate"), P(S)S ("dithioate"), "(O)NR.sub.2 ("amidate"), P(O)R, P(O)OR', CO or CH.sub.2 ("formacetal"), in which each R or R' is independently H or substituted or unsubstituted alkyl (1-20 C.) optionally containing an ether (-O-) linkage, aryl, alkenyl, cycloalkyl, cycloalkenyl or araldyl. Not all linkages in a polynucleotide need be identical. The preceding description applies to all polynucleotides referred to herein, including RNA and DNA.

Detail Description Paragraph (59):
[0104] Generation of primers suitable for extension by polymerization is well known in the art, such as described in PCT Pub. No. WO99/42618 (and references cited therein). The composite primer comprises a combination of RNA and DNA (see definition above), with the 3'-end nucleotide being a nucleotide suitable for nucleic acid extension. The 3'-end nucleotide can be any nucleotide or analog that when present in a primer, is extendable by a DNA polymerase. Generally, the 3'-end nucleotide has a 3'-OH. Suitable primers include those that comprise at least one portion of RNA and at least one portion of DNA. As shown in Example 5 (showing the relative performance of the various primers used for amplification of E. coli J gene) for one gene, composite primers can comprise a 5'-RNA portion and a 3'-DNA portion (in which the RNA portion is adjacent to the 3'-DNA portion); or 5'- and 3'-DNA portions with an intervening RNA portion. Accordingly, in one embodiment, the composite primer comprises a 5' RNA portion and a 3'-DNA portion, preferably wherein the RNA portion is adjacent to the 3'-DNA portion. In another embodiment, the composite primer comprises 5'- and 3'-DNA portions with at least one intervening RNA portion (i.e., an RNA portion between the two DNA portions). In yet another embodiment, the composite primer of the present invention comprises a 3'-DNA portion and at least one intervening RNA portion (i.e., an RNA portion between DNA portions).

Detail Description Paragraph (80):
[0125] Previously described amplification methods based on template switch oligonucleotide were restricted in the concentration of this oligonucleotide due to inhibition of hybridization of the second primer, or the second hybridization step of the same primer when the method is designed to utilize a single primer species. The methods of the invention are free of this limitation. In contrast to previously described methods using TSOs, the template switch oligonucleotide can be used at

high concentration for amplification according to the methods of the present invention. This feature ensures efficient hybridization of the oligonucleotide to the target strand, and maximizes the yield of the tri molecular complex, the substrate for primer extension and template switch. An additional attribute of this feature is the efficient hybridization of the displaced primer extension product to the template switch oligonucleotide to form a substrate for the RNA polymerase, as described.

Detail Description Paragraph (84):
[0129] In some embodiments, the 5' portion of the TSO comprises a sequence (hereinafter "propromoter sequence"), that is designed for formation of a double stranded promoter of an RNA polymerase. This embodiment of the TSO would function both as a termination sequence and to provide a promoter template. In this embodiment, the propromoter sequence of the TSO serves as a template for incorporation of a propromoter sequence (generally complementary to the propromoter sequence of the template TSO) into the primer extension product. Subsequent hybridization of a TSO comprising a propromoter sequence that is hybridizable to the propromoter sequence of the primer extension product results in formation of a double stranded promoter capable of effecting transcription by a suitable RNA polymerase. Promoter sequences that allow transcription of a template DNA are known in the art, as are methods of obtaining and/or making them. Preferably, the promoter sequence is selected to provide optimal transcriptional activity of the particular RNA polymerase used. Criteria for such selection, i.e., a particular promoter sequence particularly favored by a particular RNA polym erase, are also known in the art. For example, the sequences of the promoters for transcription by T7 DNA dependent RNA polymerase and SP6 are known in the art. The promoter sequence can be from a prokaryotic or eukaryotic source.

Detail Description Paragraph (85):
[0130] In one embodiment, the promoter sequence is adjacent to a sequence that is designed to provide for enhanced, or more optimal, transcription by the RNA polymerase used. In some embodiments, the sequence is not related (i.e., it does not substantially hybridize) to the target nucleic acid. More optimal transcription occurs when transcriptional activity of the polymerase from a promoter that is operatively linked to said sequence is greater than from a promoter that is not so linked. The sequence requirements for optimal transcription are generally known in the art as previously described for various DNA dependent RNA polymerases, such as in U.S. Pat. Nos. 5,766,849 and 5,654,142.

Detail Description Paragraph (86):
[0131] In a preferred embodiment, a segment of the 3' portion of the TSO (including the entire 3' portion that hybridizes to target) that hybridizes to the template DNA is attached to the template DNA such that displacement of the TSO by the polymerase that effects primer extension is substantially, or at least sufficiently, inhibited. Suitable methods for achieving such attachment includes techniques known in the art, such as using a cytosine analog that contains a G-clamp heterocycle modification (described in Flanagan et al., Proc. Natl. Acad. Sci. U.S.A. 1999, 96(7):3513-8); and locked nucleic acids (described, e.g., in Kumar et al., Bioorg. Med. Chem Lett. 1998, 8(16):2219-22; and Wahlestedt et al., Proc. Natl. Acad. Sci. U.S.A. 2000, 97(10):5633-8). Other suitable methods include using, where appropriate, sequences with a high GC content and/or cross-linking. Any of these methods for obtaining enhanced attachment may be used alone or in combination. Displacement of the TSO is substantially or sufficiently inhibited if the polymerase switches template from the target nucleic acid strand to the unhybridized portion of the TSO in at least about 25%, preferably at least about 50%, more preferably at least about 75%, and most preferably at least about 90%, of the events of primer extension. Substantially or sufficiently inhibited TSO displacement can also be empirically indicated if the amplification methods lead to a satisfactory result in terms of amount of the desired product. Generally, under a given set of conditions, the "modified" TSO binds more tightly to template as compared to a TSO not so modified.

Detail Description Paragraph (96):
[0141] A PTO for use in the methods and compositions of the present invention is a single-stranded polynucleotide, generally DNA, comprising a propromoter sequence that is designed for formation of a ds promoter of an RNA polymerase, and a portion

capable of hybridizing to the 3' end of the primer extension product. In a preferred embodiment, the propromoter sequence is located in the 5' portion of the oligonucleotide and the hybridizing sequence is located in the 3' portion of the oligonucleotide. In one embodiment, and most typically, the promoter and hybridizing sequences are different sequences. In another embodiment, the promoter and hybridizing sequences overlap in sequence identity. In yet another embodiment, the promoter and hybridizing sequences are the same sequence, and thus are in the same location on the PTO. In the embodiments wherein hybridization of the PTO to the primer extension product results in a duplex comprising an overhang (the 5' end of the PTO that does not hybridize to the displaced primer extension product, typically comprising all or part of the propromoter sequence), DNA polymerase fills in the overhang to create a double stranded promoter capable of effecting transcription by a suitable RNA polymerase.

Detail Description Paragraph (97):
[0142] Promoter sequences that allow transcription of a template DNA are known in the art and have been discussed above. Preferably, the promoter sequence is selected to provide optimal transcriptional activity of the particular RNA polymerase used. Criteria for such selection, i.e., a particular promoter sequence particularly favored by a particular RNA polymerase, is also known in the art. For example, the sequences of the promoters for transcription by T7 DNA dependent RNA polymerase and SP6 are known in the art. The promoter sequence can be from a prokaryotic or eukaryotic source.

Detail Description Paragraph (98):
[0143] In some embodiments, the PTO comprises an intervening sequence between a propromoter sequence and a portion capable of hybridizing to the 3' end of the primer extension product. Suitable length of the intervening sequence can be empirically determined, and can be at least about 1, 2, 4, 6, 8, 10, 12, 15 nucleotides. Suitable sequence identity of the intervening sequence can also be empirically determined, and the sequence is designed to preferably, but not necessarily, enhance degree of amplification as compared to omission of the sequence. In one embodiment, the intervening sequence is a sequence that is designed to provide for enhanced, or more optimal, transcription by the RNA polymerase used. Generally, the sequence is not related (i.e., it does not substantially hybridize) to the target nucleic acid. More optimal transcription occurs when transcriptional activity of the polymerase from a promoter that is operatively linked to said sequence is greater than from a promoter that is not so linked. The sequence requirements for optimal transcription are generally known in the art as previously described for various DNA dependent RNA polymerases, such as in U.S. Pat. Nos. 5766849 and 5654142, and can also be empirically determined.

Detail Description Paragraph (102):
[0147] DNA polymerase, ribonuclease and RNA polymerase

Detail Description Paragraph (103):
[0148] The amplification methods of the invention employs the following enzymes: a DNA polymerase, ribonuclease such as RNase H, and, optionally a DNA dependent RNA polymerase.

Detail Description Paragraph (106):
[0151] The DNA-dependent RNA polymerase for use in the methods and compositions of the present invention are known in the art. Either eukaryotic or prokaryotic polymerases may be used. Examples include T7, T3 and SP6 RNA polymerases. Generally, the RNA polymerase selected is capable of transcribing from the promoter sequence provided by the TSO or PTO as described herein. Generally, the RNA polymerase is a DNA dependent polymerase, which is preferably capable of transcribing from a single stranded DNA template so long as the promoter region is double stranded.

Detail Description Paragraph (110):
[0155] Nucleotide and/or nucleotide analogs, such as deoxyribonucleoside triphosphates, that can be employed for synthesis of the primer extension products in the methods of the invention are provided in the amount of from preferably about 50 to about 2500 .mu.M, more preferably about 100 to about 2000 .mu.M, even more preferably about 500 to about 1700 .mu.M, and most preferably about 800 to about

1500 .mu.M. In some embodiments, a nucleotide or nucleotide analog whose presence in the primer extension strand enhances displacement of the strand (for example, by causing base pairing that is weaker than conventional AT, CG base pairing) is included. Such nucleotide or nucleotide analogs include deoxyinosine and other modified bases, all of which are known in the art. Nucleotides and/or analogs, such as ribonucleoside triphosphates, that can be employed for synthesis of the RNA transcripts in the methods of the invention are provided in the amount of from preferably about 0.25 to about 6 mM, more preferably about 0.5 to about 5 mM, even more preferably about 0.75 to about 4 mM, and most preferably about 1 to about 3 mM.

Detail Description Paragraph (119):
[0164] When not linked to transcription, the amplification method of the invention provides for isothermal linear amplification of a target nucleic acid sequence. The method utilizes a single composite primer. In one embodiment, the method also employs a termination sequence, such as a blocker sequence as described in Method 2, or a TSO, as described in Method 1. Methods 1 and 2 are described below. Insofar as the linear amplification is not linked to transcription, the components and steps leading to formation of a complex comprising a promoter sequence for a DNA dependent RNA polymerase, are not included.

Detail Description Paragraph (128):
[0173] The present invention also provides methods for amplifying a target polynucleotide sequence wherein the amplified product is RNA containing the sense sequence (i.e., same sequence as target). Amplification of target nucleic acid according to Method 1, which results in the generation of a unique intermediate amplification product comprising target and template switch oligonucleotide (TSO)-related portions, provides for coupling of the linear amplification to transcription. The complex formed by the hybridization of the template switch oligonucleotide and the displaced primer extension product is a substrate for transcription by the RNA polymerase, which generates an RNA product of the same sense as the initial target sequence. Similarly, amplification of nucleic acid target according to Method 2 results in formation of a displaced primer extension product which when hybridized to the promoter template oligonucleotide forms a complex, which is a substrate for the RNA polymerase. As in Method 1, this process results in coupling of the linear amplification to transcription. The production of preferably at least about 1, more preferably at least about 50, even more preferably at least about 75, still more preferably at least about 100, and most preferably at least about 1000, RNA transcript products from each primer extension product is expected, thus leading to preferably at least about 1, more preferably at least about 50, even more preferably at least about 75, still more preferably at least about 100, and most preferably at least about 1000-fold enhancement with respect to the non-transcription linked methods of amplification.

Detail Description Paragraph (132):
[0177] The TSO-based nucleic acid amplification method of the invention employs a single composite primer, as described above. A second oligonucleotide used in the amplification method of the invention is a template switch oligonucleotide (TSO), also as described above. The amplification method of the invention employs the following enzymes: a DNA polymerase, a ribonuclease such as RNase H, and a DNA dependent RNA polymerase. The nucleic acid target to be amplified can be DNA or RNA. Amplification of an RNA target will require initial cDNA synthesis, as known in the art.

Detail Description Paragraph (134):
[0179] The single stranded target nucleic acid is combined with the composite primer, a TSO oligonucleotide, DNA polymerase, ribonuclease such as RNase H, a DNA dependent RNA polymerase, and nucleotides, such as deoxyribonucleoside triphosphates (dNTPs) and ribonuceoside triphosphates (rNTPs), in a reaction medium suitable for nucleic acid hybridization and amplification, as known in the art. Suitable reaction medium and conditions are as described above. In one embodiment, transcription is performed at a different temperature, generally lower, than that of the preceding steps. In another embodiment, all the steps of the methods are performed isothermally.

Detail Description Paragraph (139):
[0184] Complex II (FIG. 2A-C) is a substrate for both an RNA polymerase and a ribonuclease such as RNase H. The DNA dependent RNA polymerase binds to the functional ds promoter of complex II and transcribes the first primer extension product to produce a sense RNA product III (FIG. 2A-C). A ribonuclease, such as RNase H, which is specific for degradation of the RNA strand of an RNA/DNA heteroduplex, degrades the 5' portion of the primer extension product in complex II to form the tri molecular complex IV.

Detail Description Paragraph (141):
[0186] The primer extension product generated as described above is used as a template for transcription in the embodiment wherein TSO that comprises a propromoter sequence is provided. The displaced primer extension product (VIII; FIG. 2A-C) hybridizes to free TSO oligonucleotide to form the partial duplex IX (FIG. 2A-C). Complex (duplex) IX comprises a double stranded portion at one end and two non-complementary single strands respectively derived from the primer extension product and the TSO. The double stranded portion of this partial duplex contains a fully functional double stranded promoter for the DNA dependent RNA polymerase. The last binds to the promoter of the partial duplex IX and transcribes the primer extension product to form multiple copies of a sense RNA product X (FIG. 2A-C).

Detail Description Paragraph (145):
[0190] Method 2 utilizes the single composite primer, as in Method 1, as described above, a blocker sequence component which is either an oligonucleotide or an oligonucleotide analog, which, as described above, is further able to hybridize to a sequence on the same target nucleic acid strand as the single primer, and a third oligonucleotide, the promoter template (PTO), which, as described above, comprises a 3'-portion which is able to hybridize (and is preferably complementary) to the 3'-end of the displaced extension product and a 5'-portion which includes at its 5' end a sequence of a promoter for a DNA dependent RNA polyrnerase. As in the TSO described above, the sequence immediately adjacent to the promoter sequence is designed to provide for preferably optimal transcriptional activity by the RNA polymerase used in the amplification according to the method of the invention. The blocker sequence component is designed to hybridize to the target sequence at a site which is located upstream, towards the 5' end of the target, relative to the site of hybridization of the single primer. Stated alternatively, and as described above, the blocker sequence hybridizes to a segment of target nucleic acid sequence 5' of the position in the target sequence that is complementary to the 3' end of the primer extension product. The blocker sequence binds with sufficiently high affinity so as to block primer extension at the site of blocker hybridization to the target. This feature provides a strong stop for primer extension by the polymerase and defines the 3'-end of the primer extension product.

Detail Description Paragraph (147):
[0192] The single stranded nucleic acid target is combined with the single composite primer, the blocker component, the propromoter template (PTO), DNA polymerase, ribonuclease such as RNase H, a DNA dependent RNA polymerase, and nucleotides, such as NTPs (e.g., dNTPs and rNTPs), as was described for Method 1. Suitable reaction medium and conditions are as described above. In one embodiment, the transcription is performed at a different temperature, generally lower, than that of the preceding steps. In another embodiment, all the steps of the methods are performed isothermally.

Detail Description Paragraph (151):
[0196] The promoter template oligonucleotide (PTO) binds to the displaced extension product to form complex XVIII (FIG. 3A-D), by hybridization of the 3' end portion (A) of the propromoter template to the 3' end of the displaced primer extension product. As described above, the 3' end of the PTO may be blocked or not. When the 3' end of the propromoter template is not blocked, the template will be extended along the displaced primer extension product. The 3' end of the displaced product will be extended by the nucleotide (DNA) polymerase along the B portion (see FIG. 3A-D) of the hybridized propromoter template to form complex XIX, which comprises at its one end a ds promoter sequence that can be utilized by the DNA dependent RNA polymerase. Complex XIX is depicted in FIG. 3A-D as the product of hybridization of a promoter template in which the 3' end is blocked for extension by the polymerase.

Alternatively, when the 3' end of the promoter template is not blocked extension of the 3' end along the displaced primer extension product results in formation of a fully double stranded complex. DNA-dependent RNA polymerase will transcribe the extended displaced primer extension product of complex XIX, in both forms (the choice of RNA polymerase must take into account its capability to transcribe from a ds and/or ss DNA template), that is to say either the partial duplex or the fully double stranded duplex forms of the complex. Multiple copies of a single stranded RNA products are produced by this transcription step.

Detail Description Paragraph (156):
[0201] The linear isothermal amplification methods of the invention are useful, for example, for sequencing of a defined nucleic acid target sequence. The sequencing process is carried out as described for the amplification methods described herein. In addition to the nucleotides, such as natural deoxyribonucleotide tri phosphates (dNTPs), that are used for the amplification method according to the present invention, the sequencing reaction mixture also includes the appropriate nucleotide tri phosphate analogs, which may be labelled or unlabelled, that upon incorporation into a primer extension product effect termination of nucleotide polymerization. Such analogs are commonly used in other sequencing methods and are well known in the art, such as dideoxyribonucleotides. They may be labeled, e.g., with fluorochromes or radioisotopes. The labels may also be labels which are suitable for mass spectroscopy. The label may also be a small molecule which is a member of a specific binding pair, and can be detected following binding of the other member of the specific binding pair, such as biotin and streptavidin, respectively, with the last member of the binding pair conjugated to an enzyme that catalyzes the generation of a detectable signal that could be detected by methods such as colorimetry, fluorometry or chemiluminescence. All of the above examples are well known in the art. These are incorporated into the primer extension product by the polymerase and serve to stop further extension along the target sequence. The resulting truncated extension products are labeled. The accumulated multiple displaced primer extension products vary in length, according to the site of incorporation of each of the analogs, which represent the various sequence locations of a complementary nucleotide on the target sequence.

Detail Description Paragraph (157):
[0202] Analysis of the reaction products for elucidation of sequence information can be carried out using any of various methods known in the art. Such methods include gel electrophoresis and detection of the labeled bands using appropriate scanner, sequencing gel electrophoresis and detection of the radiolabeled band directly by phosphorescence such as Molecular Dynamics reader, capillary electrophoresis adapted with a detector specific for the labels used in the reaction, and the like. The label can also be a ligand for a binding protein which is used for detection of the label in combination with an enzyme conjugated to the binding protein, such as biotin-labeled chain terminator and streptavidin conjugated to an enzyme. The label is detected by the enzymatic activity of the enzyme, which generates a detectable signal. As with other sequencing methods known in the art, the sequencing reactions for the 4 nucleotide types (A, C, G, T) are carried out either in a single reaction vessel, or in separate reaction vessels (each representing 1 of the 4 nucleotide types). The choice of method to be used is dependent on practical considerations readily apparent to one skilled in the art, such as the nucleotide tri phosphate analogs and/or label used. Thus, for example, when each of the analogs is differentially labeled, the sequencing reaction can be carried out in a single vessel. The considerations for choice of reagent and reaction conditions for optimal performance of sequencing analysis according to the methods of the invention are similar to those for other previously described sequencing methods. The reagent and reaction conditions should be as described above for the linear nucleic acid amplification methods of the present invention.

Detail Description Paragraph (159):
[0204] Transcription based sequencing was previously described in, for example, Sasaki et. al., PNAS, 95:3455-3460, 1998. The inclusion of rNTPs analogs, which may be labelled or unlabelled, that upon incorporation into an RNA transcript effects termination of rNTP polymerization in the reaction mixture for the enhanced linear amplification methods will result in production of truncated RNA products, which result from blocking of the RNA polymerase at sites of incorporation of the analogs.

[redacted] rNTP analogs are known in the art. The last are incorporated opposite the [redacted]entary nucleotide on the displaced extension product in the relevant [redacted]es according to the method used (Method 1 or Method 2).

[redacted] Description Paragraph (174):
[redacted] The products of the linear nucleic acid amplification methods (DNA) and the [redacted]ced linear amplification methods (RNA) described previously are suitable for [redacted]le stranded conformation polymorphism (SSCP or rSSCP) based mutation detection. [redacted]far as the RNA product of the new amplification methods is not a substrate for [redacted]ther amplification, sequence amplification according to the new methods does not [redacted]uire the presence of agents which reduce secondary structures in the single [redacted]tranded product. Transcription-based amplification methods described by others are [redacted]rried out in the presence of agents which reduce secondary structures, such as [redacted]SO. Thus, it is anticipated that the enhanced linear amplification methods of the [redacted]resent invention can be directly linked to appropriate means for detecting single [redacted]tranded conformation polymorphism, such as an electrophoretic separation method for [redacted]he identification of specific mobility pattern of the single stranded RNA products for the elucidation of the presence of specific sequence features, or the presence of any difference in a test nucleic acid as compared to a reference nucleic acid.

Detail Description Paragraph (179):
[0224] Several techniques are well-known in the art for attaching nucleic acids to a solid substrate such as a glass slide. One method is to incorporate modified bases or analogs that contain a moiety that is capable of attachment to a solid substrate, such as an amine group, a derivative of an amine group or another group with a positive charge, into the amplified nucleic acids. The amplified product is then contacted with a solid substrate, such as a glass slide, which is coated with an aldehyde or another reactive group which will form a covalent link with the reactive group that is on the amplified product and become covalently attached to the glass slide. Other methods, such as those using amino propryl silican surface chemistry are also known in the art, as disclosed at http://www.cmt.corning.com and http://cmgm.standord.ecu/pbrownl.

Detail Description Paragraph (186):
[0231] In other embodiments, the invention provides compositions comprising (a) a composite primer, wherein the composite primer comprises an RNA portion and a 3' DNA portion (in some embodiments, the RNA portion is adjacent to the DNA portion); and (b) a termination sequence. In some embodiments, the termination sequence is a TSO. In other embodiments, the termination sequence is a blocking sequence. In some embodiments, the composite primer comprises a 5 '-RNA portion and a 3'-DNA portion (ın certain embodiments, the RNA portion is adjacent to the DNA portion). In other embodiments, the composite primer comprises 5'- and 3'-DNA portions with at least one intervening RNA portion. In some embodiments, the composition comprises (a) a composite primer; (b) a polynucleotide comprising a termination sequence; (c) a polynucleotide comprising a propromoter sequence. In some embodiments, the propromoter sequence is provided by a PTO. In other embodiments, the propromoter sequence is provided by a TSO. Any of the above compositions may further comprise template (which comprises a target sequence) and/or any of the enzymes described herein (such as DNA polymerase, RNaseH, and/or RNA polymerase). The compositions are generally in aqueous form, preferably in a suitable buffer.

Detail Description Paragraph (190):
[0235] The kits of the invention comprise one or more containers comprising any combination of the components described herein, and the following are examples of such kits. A kit may comprise any of the composite primers described herein. In some embodiments, a kit comprises two or more composite primers, which may or may not be separately packaged. In other embodiments, a kit comprises a composite primer and a termination sequence (any of those described herein). A kit may comprise a composite primer, a polynucleotide comprising a termination sequence, and a polynucleotide comprising a propromoter sequence (which may be a PTO or TSO). The composite primer may be labelled or unlabeled. Kits may also optionally include any of one or more of the enzymes described herein, as well as deoxynucleoside triphosphates and/or rıbonucleoside triphosphates. Kits may also include one or more suitable buffers (as described herein). Kits useful for nucleic acid sequencing may optionally include labeled or unlabelled nucleotide analogs that upon incorporation into a primer

extension product effect termination of nucleotide polymerization. One or more reagents in the kit can be provided as a dry powder, usually lyophilized, including excipients, which on dissolution will provide for a reagent solution having the appropriate concentrations for performing any of the methods described herein. Each component can be packaged in separate containers or some components can be combined in one container where cross-reactivity and shelf life permit.

Detail Description Paragraph (192):
[0237] The component(s) of the kit may be packaged in any convenient, appropriate packaging. The components may be packaged separately, or in one or multiple combinations. Where kits are provided for practicing the enhanced linear amplifications methods of the present invention, the RNA polymerase (if included) is preferably provided separately from the components used in the steps prior to the transcription steps.

Detail Description Paragraph (194):
[0239] The invention also provides systems for effecting the methods described herein. These systems comprise various combinations of the components discussed above. For example, in some embodiments, the invention provides a system suitable for producing target polynucleotide sequence (or amplifying target polynucleotide sequence) comprising (a) a composite primer (any of those described herein), (b) DNA polymerase; and (c) ribonuclease. In some embodiments, the system further comprises a polynucleotide comprising a termination sequence (any of those described herein). In some embodiments, the system further comprises a polynucleotide comprising a propromoter sequence (which may be a PTO or TSO) and a DNA-dependent RNA polymerase. Any of the systems embodiments may also comprise a template (target) sequence, as described herein.

Detail Description Paragraph (195):
[0240] The invention also provides reaction mixtures (or compositions comprising reaction mixtures) which contain various combinations of components described herein. In some embodiments, the invention provides reaction mixtures comprising (a) a polynucleotide template; (b) a composite primer comprising a 3' DNA portion and an RNA portion; and (c) DNA polymerase. As described herein, any of the composite primers may be in the reaction mixture (or a plurality of composite primers), including a composite primer comprises a 5' RNA portion which is adjacent to the 3' DNA portion. The reaction mixture could also further comprise an enzyme which cleaves RNA from an RNA/DNA hybrid, such as RNase H. A reaction mixture of the invention can also comprise any of the polynucleotides comprising termination sequences described herein. Another example of a reaction mixture is (a) a displaced primer extension product (and, as such, contains at its 5' end sequence complementary to the 3' DNA portion of the composite primer, but not sequences complementary to the RNA portion of the composite primer); (b) a polynucleotide comprising a propromoter sequence (for example, a PTO); and (c) RNA polymerase. Other reaction mixtures are described herein and are encompassed by the invention.

Detail Description Paragraph (210):
[0254] RNA transcription was performed at 37.degree. C. for 3 hours in 10 ul reactions containing 2.5 ul of the linear amplification reaction mixtures above, and 40 mM Tris-HCl, pH 8.5, 70 mM KCl, 5.0 mM DTT, 12 mM MgCl.sub.2, 110 ug/ml BSA, 3 mM each rNTP (ATP, UTP, CTP, GTP, Amersham), 7.5% DMSO, 1 Unit/ul rRNasin (Promega, Madison, Wis.), and 20 Units T7 RNA polymerase (Ambion, Austin, Tex.).

Detail Description Paragraph (230):
[0274] A general schematic for this amplification method is illustrated in FIG. 2A-C. The ability of IA012, IA012b, IA015, and IA015b to convert the ssDNA template into a substrate for T7 RNA polymerase was assessed by comparing the amount of RNA produced after transcription of overlap-extension products formed between a synthetic oligo product (IA009) and each of the PTO's. Synthetic oligo product IA009 is a 100-mer with the sequence of: AGTGTCCACCCCTGCCGGGATTTTAACGGACAGCG TTTTGCTGCGCTCAACACGACCATGACCATGACATTTGTTGCACGGATCTT TGATCAGCGTACCG (SEQ ID NO: 19). Overlap-extension was performed in 15 ul reactions containing 20 mM Tris-HCl, pH 8.5, 6 mM MgCl.sub.2, 1 mM each dNTP (dATP, dTTP, dCTP, dGTP), 100 nM IA009, 100 nM PTO, and 1 Unit Bca DNA polymerase. Reactions were constituted without Bca DNA polymerase, heated to 95.degree. C. then cooled over 10 minutes to 60.degree. C.

After addition of DNA polymerase, reactions were incubated at 60.degree. C. for 30 minutes. A portion (2.5 ul) of the reaction mixture was added to the standard RNA transcription reaction mixture and the transcription reactions were assessed by gel electrophoresis.

Detail Description Paragraph (246):
[0290] Reactions were assembled with all components except the two enzymes. After heating to 70.degree. C. for 10 seconds in a programmable thermal cycler (GeneAmp 9600, Perkin Elmer), reactions were cooled to 55.degree. C.-65.degree. C. Upon attaining the lower temperature, 0.05 Unit of RNase H (diluted from the 5 U/ul stock solution using a diluent/storage solution: 10 mM Tris-HCl, pH 8.5, 30% glycerol; Hybridase thermostable RNase H, Epicentre Technologies, Madison, Wis.) and 2.0 Units Bca DNA polymerase (2 U/ul; Panvera, Madison, WI) were added. The reactions were incubated at 55.degree. C.-65.degree. C. for 30 minutes. At the end of the incubation, reactions were cooled to 4.degree. C. until RNA transcription. RNA transcription was performed at 37.degree. C. for 3 hours in 10 ul reactions containing 2.5 ul of linear amplification reaction above, and 40 mM Tris-HCl, pH 8.5, 70 mM KCl, 5.0 mM DTT, 12 mM MgCl.sub.2, 110 ug/ml BSA, 3 mM each rNTP (ATP, UTP, CTP, GTP, Amersham), 7.5% DMSO, I Unit/ul rRNasin (Promega, Madison, Wis.), and 20 Units T7 RNA polymerase (Novagen, Madison, Wis.).

Detail Description Paragraph (250):
[0294] Amplification of the defined target nucleic acid sequence is carried out as described for isothermal linear amplification, as described herein. About 10.sup.2 to 10.sup.12 copies is used for template. In addition to the natural deoxyribonucleotide triphosphates (dNTPs) that are used for the amplification method, the sequencing reaction mixture includes the labeled triphosphate analogs. If each analog is uniquely labeled, all four can be added in the same reaction tube. Otherwise, if each nucleotide analog is labeled with the same label, the sequencing reactions are carried in four different reaction tubes in which each reaction mixture contains one of the nucleotide analogs. These analogs are incorporated to the primer extension product by the polymerase and serve to stop further extension along the target sequence. The resulting truncated extension products are labeled. The accumulated multiple displaced primer extension products vary in length, according to the site of incorporation of each of the analogs, which represent the various sequence locations of a complementary nucleotide on the target sequence. Analysis of the reaction products for elucidation of sequence information can be carried out by running the products on a gel. Alternatively, other methods of anlysis can be used as well. As with other sequencing methods, the sequencing reactions are carried out either in a single reaction vessel, or in separate reaction vessels. The choice of method to be used is dependent on the nucleotide triphosphate analogs used. Thus when each of the analogs is differentially labeled, the sequencing reaction can be carried out in a single vessel. The considerations for choice of reagent and reaction conditions for optimal performance of sequencing analysis according to the method of the invention are similar to those for other previously described methods.

Detail Description Paragraph (251):
[0295] The plurality of primer extension products which differ in size in accordance with the specific incorporation of elongation terminator, are size separated using any of a variety of methods known in the art. The profile of the plurality of primer extension products produced with each of the terminator analog is indicative of the nucleotide sequence of the test nucleic acid sequence.

Detail Description Paragraph (253):
[0297] Amplification of the defined target nucleic acid sequence is carried out as described for isothermal linear amplification, which involves transcription, as described herein. Either use of TSO's or PTO's may be used to append the protopromoter sequence to the product of the isothermal linear amplification. In addition to the natural ribonucleotide triphosphates (rRTPs) that are used for the enhanced linear amplification method according to the present invention, the sequencing reaction mixture also includes the appropriate labeled triphosphate analogs, which are commonly used in other sequencing methods known in the art. These are incorporated to the extension product by the RNA polymerase and serve to stop further extension along the target sequence. The resulting truncated extension

products are labeled. The accumulated multiple displaced extension products vary in length, according to the site of incorporation of each of the analogs, which represent the various sequence locations of a complementary nucleotide on the target sequence. Analysis of the reaction products for elucidation of sequence information can be carried out as stated in the above sequencing example.

Detail Description Paragraph (267):
[0311] Particle association due to hybridization of specific probes to amplification products is also used for the detection of probe hybridization. Labeled amplification products are generated and product hybridization to probes immobilized on solid surfaces is detected and recorded by computer algorithms. The generation of labeled amplification product is carried out by incorporation of labeled rNTPs during the transcription step by substituting of one of the four rNTPs by a rNTP analog, which is labeled. The label is a dye, or a small molecule such as biotin, which is then detected by binding to specific binding entity, such as labeled streptavidin. Methods for detecting probe hybridization on solid surfaces are known in the art.

CLAIMS:

2. A method for amplifying a target polynucleotide sequence comprising: (a) hybridizing a single stranded DNA template comprising the target sequence with a composite primer, said composite primer comprising an RNA portion and a 3' DNA portion; (b) hybridizing a polynucleotide comprising a termination polynucleotide sequence to a region of the template which is 5' with respect to hybridization of the composite primer to the template; (c) extending the composite primer with DNA polymerase; (d) cleaving the RNA portion of the annealed composite primer with an enzyme that cleaves RNA from an RNA/DNA hybrid such that another composite primer can hybridize to the template and repeat primer extension by strand displacement to produce displaced primer extension product; (e) hybridizing a polynucleotide comprising a propromoter and a region which hybridizes to the displaced primer extension product under conditions which allow transcription to occur by RNA polymerase, such that RNA transcripts are produced comprising sequences complementary to the displaced primer extension products, whereby multiple copies of the target sequence are produced.

19. A method of sequencing a target nucleotide sequence comprising: (a) hybridizing a single stranded DNA template comprising the target sequence with a composite primer, said composite primer comprising an RNA portion and a 3' DNA portion; (b) optionally hybridizing a polynucleotide comprising a termination polynucleotide sequence to a region of the template which is 5' with respect to hybridization of the composite primer to the template; (c) extending the composite primer to a termination site with DNA polymerase and a mixture of dNTPs and dNTP analogs, such that primer extension is terminated upon incorporation of a dNTP analog; (d) cleaving the RNA portion of the annealed composite primer with an enzyme that cleaves RNA from an RNA/DNA hybrid such that another composite primer can hybridize to the template and repeat primer extension by strand displacement, whereby multiple copies of the complementary sequence of the target sequence are produced of varying lengths; (e) analyzing the product of steps (a) through (d) to determine sequence.

20. A method of sequencing a target nucleotide sequence comprising (a) hybridizing a single stranded DNA template comprising the target sequence with a composite primer, said composite primer comprising an RNA portion and a 3' DNA portion; (b) hybridizing a polynucleotide comprising a termination polynucleotide sequence to a region of the template which is 5' with respect to hybridization of the composite primer to the template; (c) extending the composite primer with DNA polymerase; (d) cleaving the RNA portion of the annealed composite primer with an enzyme that cleaves RNA from an RNA/DNA hybrid such that another composite primer can hybridize to the template and repeat primer extension by strand displacement to produce displaced primer extension product; (e) hybridizing a polynucleotide comprising a propromoter and a region which hybridizes to the displaced primer extension product under conditions such that transcription occurs from the extension product by RNA polymerase, using a mixture of rNTPs and rNTP analogs, such that RNA transcripts are produced comprising sequences complementary to the displaced primer extension products, and such that transcription is terminated upon incorporation of an rNTP

analog, whereby multiple copies of the target sequence are produced of varying lengths; (f) analyzing the product of steps (a) through (e) to determine sequence.

WEST

Generate Collection | Print

Search Results - Record(s) 11 through 14 of 14 returned.

☐ 11. Document ID: US 4946786 A

L9: Entry 11 of 14 File: USPT Aug 7, 1990

US-PAT-NO: 4946786
DOCUMENT-IDENTIFIER: US 4946786 A

TITLE: T7 DNA polymerase

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC
Draw Desc | Image

☐ 12. Document ID: US 4942130 A

L9: Entry 12 of 14 File: USPT Jul 17, 1990

US-PAT-NO: 4942130
DOCUMENT-IDENTIFIER: US 4942130 A

TITLE: T7 DNA polymerase

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWMC
Draw Desc | Image

☐ 13. Document ID: US 4921794 A

L9: Entry 13 of 14 File: USPT May 1, 1990

US-PAT-NO: 4921794
DOCUMENT-IDENTIFIER: US 4921794 A

TITLE: T7 DNA polymerase

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWMC
Draw Desc | Image

☐ 14. Document ID: US 4795699 A

L9: Entry 14 of 14 File: USPT Jan 3, 1989

US-PAT-NO: 4795699
DOCUMENT-IDENTIFIER: US 4795699 A

TITLE: T7 DNA polymerase

transcription mixture also contains inosine 5'-triphosphate to reduce the secondary structure of the RNA product or modified ribonucleoside triphosphates, such as 4-thio UTP, 5-bromo UTP or 5'-iodo CTP to facilitate turnover of the RNA polymerase enzyme and thereby increase the amount of RNA transcript available for analysis.

Detailed Description Text (122):
Transcription is initiated in the absence or presence of modified RNA triphosphate analogs that increase the efficiency of RNA polymerase termination at such terminator sequences, such as 4-thio UTP, 5-bromo UTP or 5'-iodo CTP. The mass of the specifically terminated RNA transcripts can be detected by mass spectrometry where the observed mass of the RNA is indicative of the location of the terminator-dependent arrest of transcription. By comparing of the alignment of the sequence immediately preceding the site of transcriptional termination from several distinct genomic locations, heretofore unknown terminator sequences may be identified for different RNA polymerases.

Detailed Description Text (207):
In vitro transcription of the nicked DNA template was carried out in 20 .mu.l reactions of 40 mM Tris-HCl (pH 7.0), 6 mM MgCl.sub.2, 2 mM spermidine, 10 mM NaCl, 10 mM dithiothreitol, 1 unit/.mu.l RNasin (Promega), 5 mM rNTP, 5 .mu.Ci (.alpha.-32P) rCTP, 1 unit/.mu.l SP6 RNA polymerase (Amersham, Arlington Heights, Ill.) at 37.degree. C. for 30 minutes. Abortive and full length RNA transcripts were separated by gel electrophoresis and quantified by measuring the radioactivity of individual RNA fragments by drying the polyacrylimide gel and measuring the radioactivity as compared to a known standard using a Phospholmager (Molecular Dynamics, Inc.). The efficiency of full-length RNA transcription of a nicked DNA template was calculated as a percentage the moles of full length RNA transcribed from a DNA template containing no nicks. The nick by pass efficiency of a nicked DNA template was calculated as a percentage of the moles full-length RNA transcript and the moles of RNA transcript stalled at the nick.

Other Reference Publication (83):
Axelrod et al., "Transcription from bacteriophage T7 and SP6 RNA polymerase promoters in the presence of 3'-Deoxyribonucleoside 5'-triphosphate chain terminators", Biochemistry 245716-5723 (1985).

CLAIMS:

9. The method of claim 1, wherein the RNA polymerase is selected from the group consisting of Escherichia coli RNA polymerase, T7 RNA polymerase, SP6 RNA polymerase, T3 RNA polymerase and Q.beta. replicase.

Acad. Sci. 2232, 1979) or deazaguanosine triphosphate (deaza GTP, Mizusawa et al., 14 Nuc. Acid Res. 1319, 1986). We have found that both analogs function well with T7-type polymerases, especially with dITP in the presence of ssb. Preferably these reactions are performed with the above described genetically modified T7 polymerase, or the chase reaction is for 1-2 min., and/or at 2.degree. C. to reduce exonuclease degradation.

Other Reference Publication (132):
Axelrod et al., "Transcription from Bacteriophage T7 and SP6 RNA Polymerase Promoters in the Presence of 3'-Deoxyribonucleoside 5'-Triphosphate Chain Terminators", Biochemistry, 24:5716-5723, 1985.

WEST

Generate Collection | Print

Search Results - Record(s) 1 through 2 of 2 returned.

☐ 1. Document ID: US 20020119484 A1

L12: Entry 1 of 2 File: DWPI Aug 29, 2002

DERWENT-ACC-NO: 2002-750052
DERWENT-WEEK: 200281

TITLE: Determining mRNA expression in sample, by producing shortened amplicons from mRNA isolated from sample, electronically hybridizing amplicons to probes bound to a support, and detecting the amount of hybridized amplicons

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: JP 3331210 B2 WO 9931278 A1 AU 9919187 A EP 1038031 A1 NO 200003058 A US 6268131 B1 KR 2001033130 A JP 2002508192 W AU 745149 B

L12: Entry 2 of 2 File: DWPI Oct 7, 2002

DERWENT-ACC-NO: 1999-430042
DERWENT-WEEK: 200273

TITLE: Determining sequence of a nucleic acid by mass spectrometry

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

Generate Collection | Print

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

Generate Collection | Print

Term	Documents
REDUCE.USPT.	861451
REDUCES.USPT.	468823
SECONDARY.USPT.	336333
SEC.USPT.	125329
STRUCTURE.USPT.	1303630
STRUCTURES.USPT.	481188
(7 AND (REDUCE SAME SECONDARY SAME STRUCTURE)).USPT.	14
(L7 AND (REDUCE SAME SECONDARY SAME STRUCTURE)).USPT.	14

Display Format: TI | Change Format

Previous Page Next Page

WEST

Generate Collection | Print

Search Results - Record(s) 1 through 10 of 14 returned.

☐ 1. Document ID: US 6468523 B1

L9: Entry 1 of 14 File: USPT Oct 22, 2002

US-PAT-NO: 6468523
DOCUMENT-IDENTIFIER: US 6468523 B1

TITLE: Polypeptide compositions toxic to diabrotic insects, and methods of use

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

☐ 2. Document ID: US 6372424 B1

L9: Entry 2 of 14 File: USPT Apr 16, 2002

US-PAT-NO: 6372424
DOCUMENT-IDENTIFIER: US 6372424 B1

TITLE: Rapid detection and identification of pathogens

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

☐ 3. Document ID: US 6268131 B1

L9: Entry 3 of 14 File: USPT Jul 31, 2001

US-PAT-NO: 6268131
DOCUMENT-IDENTIFIER: US 6268131 B1

TITLE: Mass spectrometric methods for sequencing nucleic acids

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

☐ 4. Document ID: US 6251639 B1

L9: Entry 4 of 14 File: USPT Jun 26, 2001

US-PAT-NO: 6251639
DOCUMENT-IDENTIFIER: US 6251639 B1

TITLE: Methods and compositions for linear isothermal amplification of

polynucleotide sequences, using a RNA-DNA composite primer

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 5. Document ID: US 5843669 A

L9: Entry 5 of 14 File: USPT Dec 1, 1998

US-PAT-NO: 5843669
DOCUMENT-IDENTIFIER: US 5843669 A

TITLE: Cleavage of nucleic acid acid using thermostable methoanococcus jannaschii FEN-1 endonucleases

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 6. Document ID: US 5639608 A

L9: Entry 6 of 14 File: USPT Jun 17, 1997

US-PAT-NO: 5639608
DOCUMENT-IDENTIFIER: US 5639608 A

TITLE: Method for sequencing DNA using a T7-type DNA polymerase and short oligonucleotide primers

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 7. Document ID: US 5266466 A

L9: Entry 7 of 14 File: USPT Nov 30, 1993

US-PAT-NO: 5266466
DOCUMENT-IDENTIFIER: US 5266466 A

TITLE: Method of using T7 DNA polymerase to label the 3' end of a DNA molecule

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 8. Document ID: US 5173411 A

L9: Entry 8 of 14 File: USPT Dec 22, 1992

US-PAT-NO: 5173411
DOCUMENT-IDENTIFIER: US 5173411 A

TITLE: Method for determining the nucleotide base sequence of a DNA molecule

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 9. Document ID: US 5145776 A

L9: Entry 9 of 14 File: USPT Sep 8, 1992

US-PAT-NO: 5145776
DOCUMENT-IDENTIFIER: US 5145776 A

TITLE: Method of using T7 DNA polymerase to mutagenize and fill-in DNA

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 10. Document ID: US 4994372 A

L9: Entry 10 of 14 File: USPT Feb 19, 1991

US-PAT-NO: 4994372
DOCUMENT-IDENTIFIER: US 4994372 A

TITLE: DNA sequencing

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

Generate Collection | Print

Term	Documents
REDUCE.USPT.	861451
REDUCES.USPT.	468823
SECONDARY.USPT.	336333
SEC.USPT.	125329
STRUCTURE.USPT.	1303630
STRUCTURES.USPT.	481188
(7 AND (REDUCE SAME SECONDARY SAME STRUCTURE)).USPT.	14
(L7 AND (REDUCE SAME SECONDARY SAME STRUCTURE)).USPT.	14

Display Format: TI | Change Format

Previous Page Next Page

WEST

Generate Collection Print

L9: Entry 3 of 14 File: USPT Jul 31, 2001

DOCUMENT-IDENTIFIER: US 6268131 B1
TITLE: Mass spectrometric methods for sequencing nucleic acids

Brief Summary Text (10):
Transcription is initiated from the promoter by the addition of the appropriate RNA polymerase in the presence of ribonucleoside triphosphates and a selected base-specific chain terminating 3'-deoxyribonucleoside triphosphate. In preferred embodiments, the transcription mixture also contains inosine 5'-triphosphate to reduce the secondary structure of the RNA product and may further contain modified ribonucleoside triphosphates, such as 4-thio uridine 5'triphosphate (UTP), 5-bromo UTP or 5'-iodo CTP to increase the fidelity of termination and turnover of the RNA polymerase enzyme thereby increasing the amount of RNA transcript available for analysis.

Brief Summary Text (16):
Transcription is initiated in the absence or presence of modified RNA triphosphate analogs that increase the efficiency of RNA polymerase termination at such terminator sequences, such as 4-thio UTP, 5-bromo UTP or 5'-iodo CTP. In certain embodiments, nicks in one or more strand may be ligated by the addition of an appropriate nucleic acid ligase prior to initiating transcription (i.e., adding a DNA or RNA ligase). The mass of the terminated RNA transcripts is determined by mass spectrometry. The observed mass is indicative of the location of the terminator-dependent arrest of transcription and by comparing the alignment of the sequence immediately preceding the site of transcriptional termination from distinct genomic locations, terminator and attenuator sequences may be identified for different RNA polymerases.

Drawing Description Text (18):
FIG. 17 shows the nucleotide sequence of a DNA molecule (SEQ ID No: 10) assembled by hybridizing a 55-mer oligonucleotide to a complementary 25-mer oligonucleotide (SEQ ID No: 11) and a complementary 30-mer oligonucleotide ISEQ ID No: 12). The resulting double stranded DNA encodes a SP6 promoter (nt 1-18 of SEQ ID No: 10) and has a single nick in the coding strand of the molecule at nt +7 relative to the start of transcription from the SP6 promoter. The position of the nick and the start of transcription initiation from the SP6 promoter are indicated.

Detailed Description Text (23):
As used herein, RNA polymerase refers to DNA-dependent RNA polymerases and RNA-dependent RNA polymerases. Any RNA polymerase that recognizes a specific promoter sequence and is capable of initiating transcription and elongating a RNA transcript is contemplated within the scope of the term herein. Exemplary RNA polymerases that may be used in the methods provided herein include, but are not limited to those obtained from: 1) archeabacteria, such as Halobacterium, Methanobacterium, Methanococcus, Sulfolobales and Thermoplasma; 2) eubacteria, such as gram negative bacteria, e.g., Escherichia coli and strains of Salmonella and Shigella, gram positive bacteria, e.g., Bacillus subtilis and Staphlococcus aureus; 3) bacteriophages, such as T7, T3, SP6, SP6 nicked and N4; 4) DNA viruses; 5) RNA viruses, such as influenza virus; 6) plants, such as wheat; and 7) eukaryotic RNA polymerase II isolated from fungii, e.g., Saccharomyces cerevisae and higher eukaryotic organisms, e.g., mammals. Also included within the scope of the term RNA polymerase as used herein is the RNA phage Q.beta. replicase.